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FEATURES OF PREGNANCY ON THE BACKGROUND OF CHRONIC HEPATITIS B AND SARS-COV2-19 AND PREECLAMPSIA OF MODERATE SEVERITY

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Abstract. *Introdution.* The coronavirus (SARS-COV-2), a new strain of coronavirus, was first identified in Wuhan, China. Other coronavirus infections include the common cold (HCoV 229E, NL63, OC43, and HKU1), Middle East Respiratory Syndrome (MERS-CoV), and Severe Acute Respiratory Syndrome (SARS-CoV).

Aim. To analyze the peculiarities of pregnancy in the presence of two active infectious processes caused by coronavirus and hepatitis B virus, to trace the course of acute respiratory viral disease and the peculiarities of complications in this clinical case.

Materials and methods. To demonstrate the description of the clinical case, the medical history of a woman admitted to the Uzhhorod local maternity hospital was taken. The course of pregnancy, childbirth and the postpartum period of a woman is analyzed.

Research results and their discussion. The patient was admitted with complaints of dry cough, shortness of breath, increased pressure to 150/100 mm Hg. and oedema of the lower extremities. She was hospitalized in the Department of Pathology of Pregnancy KNP "Uzhgorod City Maternity Hospital" with a diagnosis of pregnancy I 27 weeks. OAA (infertility I), moderate preeclampsia, COVID - 19. Chronic hepatitis B (HBsAg carrier), minimal stage of activity. In this case, against the background of ineffective therapy, deterioration of the ultrasound picture (slowing of blood flow in the umbilical artery, signs of initial centralization of blood circulation), as well as deterioration of the general condition of the patient (pressure on the sternum, dizziness) A live premature baby weighing 800 grams was born. The Apgar score was 5/6. In the operating room, primary resuscitation of the newborn was performed and later the child was transferred to the intensive care unit for treatment. Postoperative period without complications. The mother was discharged home on the 7th day after delivery in satisfactory condition.

Conclusions. SARS CoV2 - 19 did not activate the chronic process in the liver, but triggered the mechanisms of uncontrolled preeclampsia. Of course, one case is not an evidence base for concluding the course of pregnancy against the background of chronic hepatitis and SARS CoV2-19, but it is an interesting example for further research.

Key words: SARS-CoV2-19, chronic hepatitis b, pregnancy, preeclampsia.

Особливості перебігу вагітності на фоні хронічного гепатиту В та SARS COV2-19, та прееклампсії середнього ступеня тяжкості

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Резюме. *Вступ.* Коронавірус (SARS-COV-2) – це новий штам коронавірусу, вперше ідентифікований у місті Ухань, Китай. Інші коронавірусні інфекції включають застуду (HCoV 229E, NL63, OC43 та HKU1), респіраторний синдром Близького Сходу (MERS-CoV) та тяжкий гострий респіраторний синдром (SARS-CoV).

Мета дослідження. Проаналізувати особливості перебігу вагітності за наявності двох активних інфекційних процесів, спричинених коронавірусом і вірусом гепатиту В, прослідкувати перебіг гострого респіраторного вірусного захворювання й особливості розвитку ускладнень у наведеному клінічному випадку.

Матеріали та методи. Для демонстрації опису клінічного випадку взято історію хвороби жінки, що поступила до Ужгородського місцевого пологового будинку. Проаналізовано перебіг вагітності, пологів та післяпологового періоду жінки.

Результати досліджень. Хвора поступила зі скаргами на сухий кашель, задишку, підвищення тиску до 150/100 мм рт. ст. і набряки нижніх кінцівок. Була госпіталізована у відділення патології вагітності КНП «Ужгородський міський пологовий будинок» з діагнозом: вагітність І 27 тиж. ОАА (неплідля І), прее-

клампсія середнього ступеня, COVID-19. Хронічний гепатит В (носій HBsAg), мінімальна стадія активності. У даному випадку на фоні неефективності терапії, погіршення УЗД-картини (сповільнення кровоплину в пупковій артерії, ознаки початкової централізації кровообігу), а також погіршення загального стану хворої (поява тиснучих болей за грудниною, головокружіння) було вирішено провести кесарів розтин. Народилася жива недоношена дитина вагою 800 г. Оцінка за шкалою Апгар склала 5/6. У операційній проводилася первинна реанімація новонародженого, і в подальшому дитину перевели у відділення інтенсивної терапії для лікування. Післяопераційний період без ускладнень. Породіллю виписали додому на 7 добу після пологів у задовільному стані.

Висновки. SARS CoV2-19 не призвів до активації хронічного процесу в печінці, але запустив механізми розвитку неконтрольованої прееклампсії. Звісно, один випадок не є доказовою базою для формування висновків перебігу вагітності на фоні хронічного гепатиту та SARS CoV2-19, але служить цікавим прикладом для подальшого розвитку досліджень.

Ключові слова: SARS-CoV2-19, хронічний гепатит В, вагітність, прееклампсія.

Introduction

The coronavirus (SARS-COV-2), a new strain of coronavirus, was first identified in Wuhan, China. Other coronavirus infections include the common cold (HCoV 229E, NL63, OC43, and HKU1), Middle East Respiratory Syndrome (MERS-CoV), and Severe Acute Respiratory Syndrome (SARS-CoV).

The most common ways of transmission of coronavirus are airborne. There are also data on the air way of transmission.

The pathophysiology of COVID-19 is not fully understood; however, SARS-CoV-2 has been shown to bind to angiotensin-converting enzyme 2 (ACE2) receptors in humans, suggesting that the pathogenesis is similar to that of SARS. The unique structure of the binding domain of the spiked glycoprotein receptors SARS-CoV-2 (which are responsible for the entry of the virus into host cells) provides a potentially higher binding affinity for ACE inhibitors on host cells compared to SARS-CoV. Mechanistic evidence for other coronaviruses suggests that SARS-CoV-2 may reduce ACE inhibitors, leading to toxic excessive plasma accumulation of angiotensin II, which in turn can lead to acute respiratory distress syndrome and fulminant myocarditis.

Based on the analysis of RNA sequencing data of one cell from large human physiological systems, the organs that are considered more susceptible to SARS-CoV-2 infection due to their ACE2 expression levels are the lungs, heart, oesophagus, kidneys, bladder and ileum. This may explain the extrapulmonary manifestations associated with the infection. Lower ACE-2 expression in the nasal epithelium of children <10 years of age compared to adults may explain why COVID-19 is less common in children; however, further research on this topic is needed.

The virus uses the transmembrane protease serine 2 (TMPRSS2) of the host to prime protein C and fuses the cell membranes of the virus and the host. Higher TMPRSS2 expression was observed in the nasal epithelium of blacks compared to Asians, Hispanics, whites, and people of mixed race/ethnicity, which may be a contributing factor to the greater burden of infection among blacks.

An unpublished study (not yet reviewed) found that the binding energy between the prickly protein SARS-CoV-2 and ACE inhibitors was the highest in humans of all the samples tested, indicating a unique evolution of the prickly protein SARS-CoV-2 for binding and infection of human cells expressing ACE inhibitors. A furin-like cleavage site was detected in the spiny protein of the virus; this does not exist in other SARS-like coronaviruses.

Autopsies revealed that patients who died of respiratory failure had exudative diffuse alveolar lesions with massive capillary stagnation, often accompanied by microthrombi. The formation of hyaline membranes and atypical pneumocyte hyperplasia are common. Pulmonary artery obstruction by thrombotic material was found at both macroscopic and microscopic levels. Patients also showed signs of generalized thrombotic microangiopathy. Severe endothelial damage is associated with the presence of an intracellular virus, and cell membrane damage has also been observed. Other findings included bronchopneumonia, pulmonary embolism, alveolar haemorrhage, and vasculitis. Significant growth of new blood vessels due to angiogenesis by bifurcation (intussusception) distinguishes pulmonary pathology in the case of COVID-19 from severe influenza infection.

In one autopsy study of patients, histopathological examination of brain samples showed hypoxic changes but did not reveal any encephalitis or other specific changes in the brain caused by the virus. The virus was found

in low levels in brain tissue. Another study found mild neuropathological changes, in addition, the most common finding was pronounced neuroinflammatory changes in the brain stem.

In addition, SARS-CoV-2 autopsy was often detected in the myocardium. The virus, along with inflammatory changes has been reported in the heart tissue of children with childhood inflammatory multisystem syndrome.

Evaluation of the immune infiltrate revealed a marked presence of aggregated neutrophils in the lungs and some other organs. Neutrophilic plaques, which consist of neutrophils with neutrophilic extracellular traps (NPTs) or are aggregates of NPPs and platelets, have been present in the heart, kidneys, liver, and brain. Therefore, NSAIDs may play a role in coagulopathy associated with SARS-CoV-2 infection. The disproportionate presence of aggregated neutrophils and NPP compared to the sporadic presence of the virus indicates an autonomous maladaptive immune response.

Other new findings at autopsy include pancreatitis, pericarditis, adrenal microinfarction, secondary disseminated mucormycosis, and microglial activation of the brain.

There is a hypothesis that COVID-19 is an endothelial disease. Endotheliopathy and platelet activation appear to be important features of COVID-19 in hospitalized patients and are likely to be associated with coagulopathy, critical illness, and death. Hyperviscosity has been reported in patients. It is known to damage the endothelium and is a known risk factor for thrombosis.

The potential link between hyperviscosity and thrombotic complications requires further investigation.

It is believed that genetic factors play a role in pathogenesis. A series of cases - four men with severe disease - found rare variants of the TLR7 chromosome, which are likely to cause loss of function associated with impaired interferon response.

The main clinical manifestations of the infectious process include:

- high temperature over 38 ° C (90%);
- cough, dry or with a small amount of sputum (80%); shortness of breath with BPH> 22 per minute (55%);
- myalgia, fatigue, weakness (44%);
- feeling of tightness in the chest (> 20%);
- confusion of consciousness (9%);
- headaches (8%);
- hemoptysis (5%);
- gastrointestinal symptoms, which included anorexia (83.8% of cases), diarrhoea (3 to 29% of cases), vomiting (0.8% of cases) and abdominal pain (0.4% of cases).

Hepatitis B is a viral infectious disease that affects the liver and occurs in acute or chronic form.

In highly endemic areas, hepatitis B is most often transmitted either from mother to child during childbirth (perinatal transmission) or as a result of horizontal transmission (contact with infected blood), especially between infected and uninfected children in the first five years of life. Infants infected by the mother or children infected before the age of 5 often develop a chronic infection.

Hepatitis B is also transmitted by needle pricking, tattooing, piercing, and contact with infected blood and body fluids, including saliva, menstrual and vaginal discharge, and semen. Infection can also occur through the reuse of infected needles and syringes or sharp objects in medical facilities or at home, as well as among injecting drug users. The infection can be transmitted through medical, surgical and dental procedures, tattooing, and the use of shaving blades and similar devices infected with infected blood. In addition, the hepatitis B virus can be sexually transmitted, especially in unvaccinated individuals who have multiple sexual partners.

Chronic hepatitis B develops in less than 5% of people infected in adulthood and about 95% of those infected in childhood and early childhood. The hepatitis B virus can survive outside the human body for at least seven days. During this time, the virus retains the ability to cause infection if an unvaccinated person enters the body. The duration of the incubation period of hepatitis B ranges from 30 to 180 days and averages 75 days. The virus is detected in the blood for 30-60 days after infection and can persist in the body, causing chronic hepatitis B, especially when infected in childhood or childhood.

The leading pathogenetic mechanism in HCV is a violation of the interaction of immune cells with hepatocytes. There is a deficiency of the T-system, depression of macrophages, weakening of the interferonogenesis system, lack of specific antibodygenesis against virus antigens, which ultimately violates the adequate recognition and elimination by the immune system of virus antigens on the surface of hepatocytes. Treatment does not lead to the formation of protective immunity, reinfection is possible).

The most important mechanism of persistence of HCV infection is multivariate, continuously variability of the virus, which avoids humoral and cellular immune response. Mutations in HCV epitopes, which are targets of cytotoxic T lymphocytes, lead to disorders of antigen processing and epitope recognition. The most pronounced variability with a particularly high rate of mutation is inherent in HCV genotype 1, which may explain the refractoriness of interferon therapy.

In the pathogenesis of damage to the liver and other organs in HCV infection is the presence of direct cytopathic action of the virus and the resulting immune reactions, causing not only damage to the liver but also other organs and tissues. The concept of systemic lesions in HVGS was first formulated in 1981 by Professor Aprosina ZG Possible replication of the virus outside the liver, namely in tissues of lymphoid and non-lymphoid origin. Reproduction of the virus in immunocompetent cells (lymphocytes) leads to a violation of their immunological function. Preservation of HCV in monocytes is the main cause of reinfection after liver transplantation in patients with severe hepatitis C.

The role of immunogenetic factors in the development of HCV infection was revealed (Heterozygosity for the hemochromatosis gene and the PiMZ phenotype of alpha-tantrypsin deficiency correlates with the degree of fibrosis). Among the host factors influencing the outcome and during HCV infection is the age at the time of infection, alcohol abuse, co-infection with hepatotropic viruses, lipid metabolism disorders, and others. The development of cirrhosis and hepatocellular carcinoma (HCC) is also more frequent and faster than co-infection with human immunodeficiency virus (HIV).

There are several markers for determining the degree of activity of hepatitis, namely:

- antigenic - HBsAg, НвсAg;
- serological - anti-HBs, anti-HBe, anti-HBs, anti-HBs - IgM, anti-HCV, anti-HCV - IgM;
- genetic - viral DNA or RNA.

Biochemical parameters:

- thymol test> 4 UNITS;
- ALT: at the minimum activity of increase no more than in 3 times; at moderate - from 3 to 10 times; when expressed - more than 10 times);
- bilirubin> 22 μmol / l;
- leukocytosis - 10 - 20 · 109 / l;
- alkaline phosphatase ≥ 5 IU;
- prothrombin <80%.

Ultrasound signs - focal or diffuse acoustic heterogeneity of liver tissue, changes in the shape, density and distribution of echoes, weakening of the latter in the deep parts of the liver (signs of fibrous parenchymal replacement). Changes in the vascular system of the liver, as well as the spleen, vena cava and superior mesenteric artery.

Aim

To analyze the peculiarities of pregnancy in the presence of two active infectious processes caused by coronavirus and hepatitis B virus, to trace the course of acute respiratory viral disease and the peculiarities of complications in this clinical case.

Materials and methods

To demonstrate the description of the clinical case, the medical history of a woman admitted to the Uzhhorod local maternity hospital was taken. The course of pregnancy, childbirth and the postpartum period of a woman is analyzed.

Research results and their discussion

The patient was admitted with complaints of dry cough, shortness of breath, increased pressure to 150/100 mm Hg. and oedema of the lower extremities. She was hospitalized in the Department of Pathology of Pregnancy KNP "Uzhgorod City Maternity Hospital" with a diagnosis of pregnancy I 27 weeks. OAA (infertility I), moderate preeclampsia, COVID - 19. Chronic hepatitis B (HBsAg carrier), minimal stage of activity. Antihypertensive treatment was prescribed, which did not give a significant effect, there were several jumps in blood pressure to 180/110 mm Hg. Laboratory: General blood sample - anemia. Genera urine sample - proteinuria, leukocyturia, erythrocyturia (fresh erythrocytes). Coagulogram: thrombocytopenia. Blood biochemistry: proteinemia, in particular, decreased albumin, ALT and AST - within normal limits. According to the protocol of the Ministry of Health "Management of pregnant women with chronic hepatitis", childbirth in chronic hepatitis is carried out through the natural birth canal. Cesarean section is performed according to obstetric indications. In this case, against the background of ineffective therapy, deterioration of the ultrasound picture (slowing of blood flow in the umbilical artery, signs of initial centralization of blood circulation), as well as deterioration of the general condition of the patient (pressure

on the sternum, dizziness) A live premature baby weighing 800 grams was born. The Apgar score was 5/6. In the operating room, primary resuscitation of the newborn was performed and later the child was transferred to the intensive care unit for treatment. Postoperative period without complications. The mother was discharged home on the 7th day after delivery in satisfactory condition.

It is known that underdevelopment of the spiral arterioles of the placenta can reduce uteroplacental blood flow at a later date. Also, the pathogenesis of preeclampsia includes genetic abnormalities of chromosome 13, immune disorders, ischemia or placental infarction. Free radical-induced lipid peroxidation of cell membranes may also contribute to the development of preeclampsia.

One of the leading theories of the development of preeclampsia is the immune theory. It is believed that in the body of a pregnant woman is the formation of antibodies in response to the penetration into the bloodstream of fetal antigens. As a result, there is the formation of circulating immune complexes, the circulation of which in the blood and deposits in the tissues leads to the launch of complex immunological mechanisms with the development of acute endotheliosis and activation of endothelial cells. The increase in the circulation time of immune complexes (IR) leads to the activation of the adhesive aggregation function of platelets, microthrombosis, increased permeability of the vascular wall. With an excess of antigens and violation of their neutralization, defective IRs are formed. They are the most active mediators of cell damage. As a result of the antigen-antibody interaction, a large number of reactive oxygen species are formed, which are able to oxidize and destroy lipid molecules, induce changes in protein structure, which in turn leads to impaired cell membrane permeability, organ destruction and multiorgan failure.

Therefore, we can say that the pathogenesis of coronavirus infection and preeclampsia is somewhat similar, and therefore there is an assumption that the presence of coronavirus infection during pregnancy and the predisposition of this patient to the development of preeclampsia deepens the development of the latter and leads to uncontrolled control. This explains the course of this obstetric complication in pregnant women.

Conclusions

SARS CoV2 - 19 did not activate the chronic process in the liver, but triggered the mechanisms of uncontrolled preeclampsia. Of course, one case is not an evidence base for concluding the course of pregnancy against the background of chronic hepatitis and SARS CoV2-19, but it is an interesting example for further research.

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